IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NOVO NORDISK INC. and NOVO NORDISK A/S,	)	
Plaintiffs,	)	
v.	)	C.A. No. 19-1551 (CFC)
MYLAN INSTITUTIONAL LLC,	)	
Defendant.	)	

JOINT CLAIM CONSTRUCTION BRIEF

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TABLE OF CONTENTS

Page

TABLE OF CONTENTS
(Continued)

Page

TABLE OF CONTENTS
(Continued)

Page

TABLE OF AUTHORITIES

Page(s)

CASES

TABLE OF AUTHORITIES
(Continued)

Page(s)

TABLE OF AUTHORITIES
(Continued)

Page(s)

TABLE OF AUTHORITIES
(Continued)

Page(s)

STATUTES AND RULES

I. INTRODUCTION

A. Plaintiffs' Opening Position

Plaintiffs Novo Nordisk Inc. and Novo Nordisk A/S (collectively, "Novo Nordisk") submit this Opening Claim Construction Brief pursuant to the Court's November 18, 2019 Scheduling Order (D.I. 16).

This case concerns Novo Nordisk's blockbuster diabetes drug Victoza®, which Defendant Mylan Institutional LLC ("Mylan") seeks to copy and sell before the expiration of Novo Nordisk's patents covering the drug. There are seven patents-in-suit, but only one is at-issue in these claim construction proceedings: U.S. Patent No. 8,114,833 ("the '833 patent"), which covers the improved injectable formulation used with Victoza®.

The claim construction dispute is limited to three preambles of certain method claims, and whether each preamble must be considered as a limitation of the claim (as Novo Nordisk proposes) or can be ignored (as Mylan proposes). These preambles are vital limitations because they recite the "essence" of the claims: reducing undesirable deposits and troublesome clogging of injection devices by using propylene glycol as the isotonicity agent, a step performed only for the reasons stated by the preambles. Without them, the manipulative step of the claims ("replacing the isotonicity agent previously utilized in said formulation

with propylene glycol") becomes a meaningless academic exercise that serves no purpose.

As documented in the specification, the inventors discovered that a widely used "isotonicity agent," mannitol, was causing undesirable deposits on their production equipment, deposits in their final drug product, and clogging of the injection needles used to administer it. In search of a solution, the inventors conducted a variety of studies, including synthesizing fourteen different formulations, each containing a different chemical to adjust tonicity, and testing them in several rounds of experiments. In the end, they discovered that one particular chemical, propylene glycol, was unexpectedly the best at reducing deposits on production equipment, deposits in the final product, and clogging of injection devices. So, the inventors replaced the isotonicity agent they had previously used (mannitol) with propylene glycol and claimed in their patent methods of reducing deposits and clogging by doing so. This is the "essence" of their invention, which is captured in the preambles in question here.

Novo Nordisk's proposed construction that each preamble is limiting, and cannot be ignored, is consistent with the controlling intrinsic evidence, including the claims themselves, as understood by a person of ordinary skill in the art. It also comports with controlling caselaw, which prescribes that a preamble embodying the claim's "*raison d'etre*" or "essence" is limiting, as is the case here. In contrast,

Mylan's proposed construction that the preambles are nonlimiting ignores the invention as a whole, which is directed to methods of reducing deposits and clogging. Without its preamble, each claim-at-issue would lack meaning and purpose—the claims would simply be directed to replacing a previously utilized isotonicity agent with propylene glycol. That would discount the inventors' innovative steps of identifying the problem of deposits and clogging, as well as the solution that is achieved by replacing the previously used isotonicity agent with propylene glycol.

B. Defendant's Answering Position

Pursuant to the Court's Scheduling Order (D.I. 16), Defendant Mylan Institutional LLC ("Mylan") submits this Answering Claim Construction Brief in response to Plaintiffs Novo Nordisk Inc. and Novo Nordisk A/S's (collectively, "Plaintiffs") Opening Claim Construction Brief.

U.S. Patent No. 8,114,833 ("the '833 patent") is directed towards pharmaceutical formulations and methods of preparing pharmaceutical formulations containing glucagon-like peptide-1 ("GLP-1") agonists. At issue here is whether the preambles of independent claims 23, 26, and 29, which do nothing more than describe the intended results of the claimed methods, are claim limitations. The intrinsic evidence and a wealth of authority show that these preambles are not limiting.

C. Plaintiffs' Reply Position

Mylan takes several fatal missteps to argue that the preambles at issue are non-limiting, from misstating Federal Circuit precedent and cherry-picking from the specification, to ignoring the dependent claims and the clear antecedent language found in each of the preambles. Moreover, Mylan fails to account for the parties' agreed upon construction of the "replacing" claim terms in the bodies of the claims at issue. Mylan's flawed analysis fails to show that the preambles at issue are non-limiting. Instead, the intrinsic evidence and controlling Federal Circuit authority support Novo Nordisk's position that each preamble is limiting.

The specification as a whole makes clear what "the inventors actually invented and intended to encompass by the claim," and the method invented is recited in the preambles. *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1347 (Fed. Cir. 2002) (internal quotation omitted); *see also Bicon, Inc. v. Straumann Co.*, 441 F.3d 945, 952 (Fed. Cir. 2006). The specification documents the inventors' work in identifying the problem of deposits and clogging in GLP-1 agonist formulations containing mannitol and later discovering that a particular chemical, propylene glycol, unexpectedly reduced deposits and clogging in such formulations. And viewed in its entirety, the specification makes clear that the essence of the claimed inventions is directed to reducing deposits on production

equipment, deposits in the final product, and clogging of injection needles in GLP-1 agonist formulations by using propylene glycol.

The language of the preambles, in turn, give "life, meaning, and vitality" to the claims, showing that they are limiting pursuant to controlling Federal Circuit precedent. Put another way, review of the specification and claim language show that the preambles set out the "essence" or "raison d'etre" of the claimed invention. Mylan summarily dismisses Novo Nordisk's application of Federal Circuit precedent to the claim language at issue, and, without conducting the "life, meaning, and vitality" inquiry, conflates it with the alternative inquiry into whether a preamble recites "essential structure or steps." *Infra* at 36-37. But the "essential structure or steps" inquiry likewise shows that the preambles are limiting because they provide a framework for the claimed inventions, i.e., reducing deposits in production equipment, reducing deposits in the final product, and reducing clogging in needles.

D. Defendant's Sur-Reply Position

Nothing in Plaintiffs' reply renders the statements of intended results recited in the preambles of claims 23, 26, and 29 limitations. The Court should reject Plaintiffs' attempt to turn intended results into method steps, at least because Plaintiffs concede that the preambles identify the "intended objective" of the

claimed methods. *Infra* at 56. The Court should hold that the preambles are nonlimiting statements of intended results.

II. BACKGROUND

A. Plaintiffs' Opening Position

1. The '833 Patent

Injectable formulations often contain "isotonicity agents," which adjust the formulation's osmotic pressure to match that of the injection site in the body. *See Novo Nordisk Inc. v. Mylan Institutional LLC*, No. 19-1551, D.I. 41, Ex. B, '833 patent at col.1, ll.30-34; *see also* McGraw-Hill Concise Dictionary of Modern Medicine (2002)[1] (defining "isotonic" as "[r]eferring to uniformity of osmotic pressure"). Using an injectable formulation that is not isotonic with the body at the injection site can be painful and cause other side effects. REMINGTON'S PHARMACEUTICAL SCIENCES, Chapter 79 (18th ed. 1990) (Ex. A[2]) at MI-LIRA0013812 ("Solutions that differ from the serum in tonicity generally are stated to cause tissue irritation, pain on injection and electrolyte shifts, the effect depending on the degree of deviation from tonicity.").

The '833 patent explains that "one of the more common isotonic agents used in such formulations is mannitol," but the inventors "observed that mannitol causes

[1] Available at: https://medical-dictionary.thefreedictionary.com/isotonic (May 29, 2020).

[2] Exhibits cited herein are included within the parties' Joint Appendix.

problems during . . . production," including "deposits in the production equipment and in the final product," as well as "clogging of [the] injection devices." D.I. 41, Ex. B, '833 patent at col.1, ll.30-45. The inventors found that deposits "increase the need to clean the filling equipment during production of the formulation" which "results in reduced production capability." *Id.* at col.1, ll.36-39. "Such deposits also result in reduced yield of the final product." *Id.* at col.1, ll.39-40. Finally, the inventors also observed that "the presence of mannitol results in clogging of injection devices." *Id.* at col.1, ll.42-45. So the inventors embarked on a series of screening studies to "identify an alternative isotonic agent." *Id.* at col.1, ll.46-49. They prepared fourteen different formulations—one with mannitol, and the others with different chemicals to adjust tonicity—and compared them in several tests: (1) the "drop test" to examine whether droplets of the experimental formulations contained deposits upon drying; (2) the "clogging test," to assess clogging of the injection needle; and (3) the "simulated filling" test, to determine which experimental formulations caused deposits on filling equipment. *Id.* at col.16, ll.5-30; col.16, l.60 – col.18, l.8.

As illustrated in the specification, the experimental results pointed to propylene glycol, which "reduced deposits in production equipment and in the final product" and "reduced clogging of the injection devices relative to formulations containing other isotonicity agents," and also created no stability,

microbial, or toxicity concerns. *Id.* at col.1, ll.53-57; col.3, ll.39-48; col.18, ll.10-67. The inventors next prepared formulations of mannitol and propylene glycol for "head to head comparison studies," and again found propylene glycol to be superior during clogging tests and simulated filling tests. *Id.* at col.18, ll.58-59 ("head to head comparison studies"), col.19, l.1 – col.20, l.5 ("Preparation of Formulations" and results of comparison studies).

Accordingly, the inventors discovered that propylene glycol formulations were "optimal for production and for use in injection devices since they exhibit reduced deposits . . . and reduced clogging" as well as reduced deposits in the final product. *Id.* at col.1, ll.53-57; col.13, ll.30-35; *see also id.* at [54]. And the specification highlights that the claimed inventions are directed to methods of reducing clogging of injection devices, reducing deposits on the production equipment, and reducing deposits in the final product by replacing the previously used isotonicity agent with propylene glycol. *Id.* at Abstract; col.1, ll.53-57. The inventors put their discovery to use by using propylene glycol as the isotonicity agent in Victoza®.

B. Defendant's Answering Position

1. The Products at Issue

Plaintiffs market Victoza®, an injection solution containing liraglutide (a GLP-1 agonist). Mylan submitted an abbreviated new drug application seeking

FDA approval for a lower-cost generic liraglutide injection solution.

2. U.S. Patent No. 8,114,833

The '833 patent describes and claims pharmaceutical formulations containing GLP-1 agonists and excipient materials, such as substances that affect the isotonicity[3] of the formulations ("isotonicity agents"), and methods for manufacturing the disclosed formulations. *See generally* D.I. 41-2 ('833 patent). The use of isotonicity agents in formulations containing peptides generally, and GLP-1 agonists specifically, was widely known before the effective filing date of the '833 patent. *See generally* D.I. 41-2 ('833 patent); Int'l Patent Application Publ'n No. WO 03/002136 by Flink (Ex. 1); REMINGTON'S PHARM. SCI. (Alfonso R. Gennaro et al. eds., 18th ed. 1990) (Ex. 2).

Claims 23, 26, and 29 each recite the identical method step of "replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml." *See* D.I. 41-2 ('833 patent) at 24:7-13, 26-32, 45-50. Claims 23, 26, and 29 are identical, except for their bolded phrases shown below:

[3] Tonicity refers generally to the osmotic pressure of a solution relative to the osmotic pressure of bodily fluids. Ex. 2 at 1462. More specifically, tonicity refers to the effect that a solution has on the amount of water that cells gain or lose upon contact with the solution. *Id*. Solutions are isotonic "if there is no net gain or loss of water by the cell, or other change in the cell when it is in contact with that solution." *Id*.

> 23. A method for reducing **deposits on production equipment during production of** a GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer.
>
> 26. A method for reducing **deposits in the final product during production of** a GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer.
>
> 29. A method for reducing **the clogging of injection devices by** a GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer.

Id. at 24:7-13, 26-32, 45-50 (emphases added).

3. Prosecution History

Claims 36, 39, and 42, as numbered during prosecution, contained the same preambles at issue here and ultimately issued as claims 23, 26, and 29, respectively. Ex. 3 May 17, 2006 Transmittal of New Application at NNVICT-MYL_00002150-51. As originally filed, the claims recited a "peptide" generically (rather than a GLP-1 agonist, specifically) and did not recite a "disodium phosphate dihydrate buffer." *Id*. The Examiner rejected the as-filed claims as anticipated by a patent application issued to Knudsen. Ex. 4 (June 25, 2009 Office Action). The Examiner explained that Knudsen taught "a pharmaceutical

formulation comprising a peptide and propylene glycol." *Id*. at NNVICT-MYL_00002600. The Examiner further explained that "[w]ith respect to claims 36-44, the effect of reducing deposits on production equipment is inherent to the prior art of Knudsen *et al.* because the compositions and methods of making them taught by the prior art are identical to the claimed invention." *Id*. at NNVICT-MYL_00002601-02.

In response, Plaintiffs amended claims 36, 39, and 42 to replace "peptide" with a "GLP-1 agonist" and further narrowed the claims to require that the formulations comprise "a disodium phosphate dehydrate [*sic*, dihydrate] buffer." D.I. 41-6 (Nov. 18, 2009 Response to Final Office Action). Plaintiffs' amendments as submitted are shown below:

> 36. (Currently Amended) A method for reducing deposits on production equipment during production of a ~~peptide~~ GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dehydrate buffer.

Plaintiffs explained that these amendments overcame the Examiner's rejection because the cited art did not teach a pharmaceutical formulation comprising a "GLP-1 agonist, about 1 mg/ml to about 100 mg/ml propylene glycol and a disodium phosphate dehydrate [*sic*] buffer, wherein said formulation has a pH of from about 7.0 to about 10.0." *Id*. at NNVICT-MYL_00002617. And,

Plaintiffs asserted that Knudsen also did not "mention a composition comprising a disodium phosphate dehydrate [*sic*] buffer, a method of preparing such or method of reducing deposits or clogging." *Id.* Thereafter, the Examiner allowed the claims to issue because the prior art allegedly did not disclose a formulation with a disodium phosphate dihydrate buffer:

> The rejection of claims 1-19, 22-28, and 30-44 under 35 U.S.C. 102(e) as being anticipated by Knudsen … is overcome by the amendment … Knudsen et al. teaches phosphate buffer which is generic to the species disodium phosphate dihydrate buffer now claimed. Therefore, the claims are not anticipated by Knudsen et al.

D.I. 41-6 (Notice of Allowability) at NNVICT-MYL_00002661. The Examiner said nothing about the claim preambles. Indeed, these preambles were recited in the claims from the outset, including when they were originally rejected. Thus, Plaintiffs and the Examiner each understood that the patent was allowed based on the claim amendments limiting the claims to formulations and methods that included a disodium phosphate dihydrate buffer.

III. AGREED UPON CONSTRUCTIONS

The parties agree that the following terms have the constructions set forth below (D.I. 41).

AGREED UPON CONSTRUCTION FOR "ISOTONIC AGENT" AND "ISOTONICITY AGENT"		
Term	**Relevant Patent and Affected Claims**	**Parties' Proposed Construction**
"isotonic agent"	'343 Patent at claim 29 '618 Patent at claims 1, 6, 13, and 14	Synonymous such that they have the same meaning in each of the '343 Patent, '618 Patent, and '833 Patent.
"isotonicity agent"	'833 Patent at claims 23-26 and 28-31	

CLAIM TERMS AGREED UPON FROM THE *TEVA* LITIGATION IN U.S. PATENT NO. 9,265,893		
Term	**Affected Claims**	**Parties' Proposed Construction**
"driving part"	1-6	"a part that transfers force from the push button"
"pivot bearing"	1-6	"a bearing that supports an end of a rotating shaft subject to an axial load"
"radial bearing"	2-4	"a bearing that supports a load on a shaft that is perpendicular to the axis of rotation"

CLAIM TERMS AGREED UPON FROM THE *TEVA* LITIGATION IN U.S. PATENT NO. RE 41,956		
Term	**Affected Claims**	**Parties' Proposed Construction**
"driver"	2	"a part that transfers force from the injection button"

"track"	2	"a path along which a part moves"
"track follower"	2	"a part that moves along a path"
"track having a length"	2	"the length of the track that the track follower can move along"

CLAIM TERMS AGREED UPON FROM THE *TEVA* LITIGATION IN U.S. PATENT NO. 8,114,833		
Term for Construction	**Affected Claims**	**Parties' Proposed Construction**
"about"	1, 5, 6, 7, 16, 20, 21, 22	When used in connection with pH, "[plus] or [minus] 0.1 pH units from [the stated number]"
"replacing the isotonicity agent previously utilized in said formulation with propylene glycol"	23, 26, 29	"Having a first formulation that utilized an isotonicity agent other than propylene glycol and having a second formulation wherein the isotonicity agent used in the first formulation is substituted or replaced with propylene glycol"
"the propylene glycol-containing formulation relative to that observed for the formulation containing the previously utilized isotonicity agent"	24, 30	"Having a first formulation that utilized an isotonicity agent other than propylene glycol and having a second formulation wherein the isotonicity agent used in the first formulation is substituted or replaced with propylene glycol"
"the isotonicity agent to be replaced by propylene glycol"	25, 28, 31	"Having a first formulation that utilized an isotonicity agent other than propylene glycol and having a second formulation wherein the isotonicity agent used in the first formulation is substituted or replaced with propylene glycol"

IV. DISPUTED CONSTRUCTIONS

A. Plaintiffs' Opening Position

1. "A Method For Reducing Deposits on Production Equipment During Production of a GLP-1 Agonist Formulation"

a. The Preamble Gives "Life, Meaning, and Vitality" to the Claims and Is an Express Limitation

Term	Claims	Novo Nordisk's Construction	Mylan's Construction
"A method for reducing deposits on production equipment during production of a GLP-1 agonist formulation"	23, 24, 25	The phrase is an express limitation of claim 23 and it carries its plain and ordinary meaning.	Nonlimiting preamble

"A claim preamble has the import that the claim as a whole suggests for it." *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305 (Fed. Cir. 1999) (citation omitted). "If the claim preamble, when read in the context of the entire claim, recites limitations of the claim, or, if the claim preamble is necessary to give life, meaning, and vitality to the claim, then the claim preamble should be construed as if in the balance of the claim." *Id.* (citations omitted).

A preamble is a limiting, necessary component of the claim if "there is no meaningful distinction to be drawn between the claim preamble and the rest of the claim." *Id.* In other words, the preamble is limiting where "the claim drafter choos[es] to use both the preamble and the body to define the subject matter of the

claimed invention." *Eaton Corp. v. Rockwell Int'l Corp.*, 323 F.3d 1332, 1340 (Fed. Cir. 2003). The "preamble language will limit the claim if it recites not merely a context in which the invention may be used, but the essence of the invention without which performance of the recited steps is nothing but an academic exercise." *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 320 F.3d 1339, 1345 (Fed. Cir. 2003); *Griffin v. Bertina*, 285 F.3d 1029, 1033 (Fed. Cir. 2002). In order to determine whether a preamble is a limitation, courts assess the claims, specification, and prosecution history. *Applied Materials, Inc. v. Advanced Semiconductor Materials Am., Inc.*, 98 F.3d 1563, 1572-73 (Fed. Cir. 1996).

"A method for reducing deposits on production equipment during production of a GLP-1 agonist formulation," should be construed as an express limitation of claims 23-25. "Reducing deposits on production equipment" is the "*raison d'etre* of the claimed method itself." *Boehringer Ingelheim*, 320 F.3d at 1345. As demonstrated by the claims, the specification, and the prosecution history, the preamble gives "life and meaning" to the later claimed process of "replacing the isotonicity agent previously utilized in said formulation with propylene glycol." *See Griffin*, 285 F.3d at 1033.

b. The Claim Language Supports a Limiting Construction

The fundamental purpose of the methods of claims 23-25 is to reduce deposits on production equipment. *See, e.g.*, D.I. 41, Ex. B, '833 patent at claim 23 ("A method for reducing deposits on production equipment during production of a GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer."). That purpose is recited in the preambles to the claims. Without those preambles, the claims reduce to nothing more than merely replacing a previously used isotonicity agent with propylene glycol—an action that is a meaningless academic exercise with no purpose in isolation. *Boehringer Ingelheim*, 320 F.3d at 1345; *Griffin*, 285 F.3d at 1033. As further evidence that the preambles must be considered as express limitations, without them, the bodies of independent claims 23, 26, and 29 each recite the exact same invention. *See* D.I. 41, Ex. B, '833 patent, claims 23, 26, & 29.

c. The Specification Reinforces a Limiting Construction

The specification of the '833 patent also demonstrates that the preamble is an express limitation and a necessary component of claims 23-25. The specification explains that the inventors observed that mannitol caused problematic

deposits on production equipment during production of peptide formulations. D.I. 41, Ex. B, '833 patent at col.1, ll.30-45; *see also supra* at Section II.A.1. The deposits prompted the inventors to conduct a number of simulated filling tests with fourteen possible chemicals to adjust the tonicity of the formulation, including propylene glycol, in order to discover if another chemical alleviated the problem. D.I. 41, Ex. B, '833 patent at Examples 1-2. After performing these simulated filling tests, which included a head-to-head comparison between mannitol and propylene glycol, the inventors discovered that propylene glycol reduced deposits in the production equipment during production of a GLP-1 agonist formulation. *Id.* In discussing the results of the simulated filling tests in Examples 1 and 2, the specification highlights that propylene glycol reduces deposits on the production equipment. *Id.*; *see also Sanofi Mature IP v. Mylan Labs., Ltd.*, 757 F. App'x 988, 993 (Fed. Cir. 2019) (finding that the example disclosed in the specification emphasizes that the preamble is "an important aspect of the invention" and thus, supports the finding that the preamble is limiting).

The specification states that the inventors concluded that GLP-1 agonist formulations containing propylene glycol were "optimal for production and for use in injection devices since they exhibit reduced deposits." D.I. 41, Ex. B, '833 patent at col.1, ll.53-57. Thus, the specification emphasizes that reducing deposits on the production equipment is the "essence" of the claimed invention. *See, e.g.*,

id. at Abstract; col.1, ll.15-57; col.2, ll.35-45; col.3, ll.1-30; col.3, ll.39-48; col.13, ll.30-35; col.14, ll.16-55; Examples 1-2; Figures 5 & 6. Therefore, the preambles should be construed as limitations. *Boehringer*, 320 F.3d at 1345.

d. The Prosecution Further Supports a Limiting Construction

The prosecution history also supports construing the preambles as limitations of claims 23-25. In overcoming an obviousness rejection of those claims, applicants stressed that the prior art did not mention "a method of reducing deposits." *See* Ex. B at NNVICT-MYL00002617 ("[N]either the Specification, nor any of the examples in [the prior art reference in question] mention . . . [a] method of reducing deposits or clogging."); Ex. C at NNVICT-MYL00002661. By expressly relying on the preamble to distinguish the claimed invention over the prior art, applicants made clear that the preamble to claims 23-25 is limiting. *See Invitrogen Corp. v. Biocrest Mfg., L.P.*, 327 F.3d 1364, 1370 (Fed. Cir. 2003).

e. Preambles Like Those At-Issue Here Have Been Found Limiting

In *Boehringer Ingelheim*, the Federal Circuit found the preamble ("[a] method of *growing and isolating* swine infertility and respiratory syndrome virus, ATC-VR2332") limiting because, "[d]ivorced from the process of growing and isolating virus, the claimed method reduces to nothing more than a process for producing [certain effects in cells]—a process whose absence of fathomable utility

rather suggests the academic exercise." *Id.* at 1345 (emphasis added). Thus, the term "isolating" was not merely a circumstance in which the method may be useful, but rather "the *raison d'etre* of the claimed method itself," and the preamble was therefore a limitation of the claim. *Id.* at 1345.

Likewise, in *Griffin*, the Federal Circuit found the preamble ("*diagnosing* an increased risk for thrombosis of a genetic defect causing thrombosis") limiting because diagnosis was "the essence of this invention" and gave "life and meaning" to the manipulative steps. *Id.* at 1033 (emphasis added). The Federal Circuit specifically noted that the manipulative steps of (a) testing the nucleic acid obtained from the test subject and (b) assaying for the presence of a point mutation were "merely academic exercises" without the preamble. *Id.* And without the preamble's stated objective to diagnose thrombosis, the remaining steps would have been "empty language" with "no purpose." *Id.*

As in *Boehringer Ingelheim* and *Griffin*, the manipulative step of claims 23-25 ("replacing the isotonicity agent previously utilized in said formulation with propylene glycol") would be a meaningless academic exercise with no purpose absent the intended objective of the preamble ("reducing deposits on production equipment."). *See also Vizio, Inc. v. ITC*, 605 F.3d 1330, 1341 (Fed. Cir. 2010) (the claims "would have little meaning without the intended objective of decoding"

because it not "only add[s] an intended use, but rather, states an essential limitation to the claims." (internal citation omitted)).

f. The Preamble Is Limiting For the Additional Reason That It Provides Antecedent Basis

A preamble may be considered a necessary component of the claimed invention "[w]hen limitations in the body of the claim rely upon and derive antecedent basis from the preamble." *Eaton Corp.*, 323 F.3d at 1339; *see also Sanofi Mature IP,* 757 F. App'x at 993 ("[T]here is a direct link between the claim as a whole and the preamble, which provides an antecedent basis. . . ."). That is, a preamble is considered limiting if a later claim limitation would have no basis without reference to the preamble. *See, e.g.*, *Rapoport v. Dement*, 254 F.3d 1053, 1059 (Fed. Cir. 2001) ("[W]ithout treating the phrase 'treatment of sleep apneas' as a claim limitation, the phrase 'to a patient in need of such treatment' would not have a proper antecedent basis.").

Limitations in the bodies of the claims-at-issue, including "*said method* comprising replacing the isotonicity agent previously utilized in *said formulation* with propylene glycol" and "*said GLP-1 agonist formulation*" derive antecedent basis from their preambles. *See, e.g.*, D.I. 41, Ex. B, '833 patent at claims 23, 26, and 29 (emphasis added). The methods and formulations referenced in the bodies of claims 23, 26, and 29 are the same ones initially recited in the preambles. Consideration of the preamble is thus required to paint a complete picture of the

claimed invention. *See Eaton Corp.*, 323 F.3d at 1339-40. When the preamble is ignored, the "formulations" recited in the bodies of the claims could be any formulation. Only when the preamble is considered is it understood that they refer back to the particular "GLP-1 agonist formulation" recited in the preambles. *See Eaton Corp.*, 323 F.3d at 1339-40; *Sanofi Mature IP*, 757 F. App'x at 993-94.

Additionally, the "wherein the *reduction*" clauses recited in dependent claims 24, 27, and 30 refer back to the preambles of the claims from which they depend, which recite "methods of *reducing* [deposits and clogging]." *See* D.I. 41, Ex. B, '833 patent, claims 23-24, 26-27, & 29-30 (emphases added). Without the methods recited in the preambles, the "wherein" clauses of claims 24, 27, and 30 lack antecedent basis. *See Eaton Corp.*, 323 F.3d at 1339; *Sanofi Mature IP,* 757 F. App'x at 993-94.

Absent the preambles, the claims do not define the entirety of the claimed inventions, with several limitations lacking antecedent basis. For this additional reason, the preambles are limiting. *See Eaton Corp.,* 323 F.3d at 1339; *Sanofi Mature IP*, 757 F. App'x at 993-94.

g. The Court Should Reject Mylan's Non-Limiting Construction

Mylan may argue that none of the preambles of the disputed claims are limiting because they allegedly recite only statements of purpose and intended result (i.e., reducing deposits on production equipment, reducing deposits in the

final product, and reducing clogging in injection needles). Not so. The preambles recite essential limitations. Each preamble gives not only purpose, but meaning, to the step of replacing the previously used isotonicity agent with propylene glycol. *See Boehringer Ingelheim*, 320 F.3d at 1345; *Griffin*, 285 F.3d at 1033. Without the preambles, claims 23-25, 26, 28, and 29-31 are structurally incomplete inventions. *See, e.g.*, *Vizio, Inc.*, 605 F.3d at 1340; *Sanofi Mature IP*, 757 F. App'x at 882. Mylan's proposed constructions as nonlimiting preambles cannot be correct.

Mylan's construction cannot be correct for the additional reason that, by ignoring the preambles, independent claim 23 would recite the same invention as claims 26 and 29. Meanwhile, Novo Nordisk's construction preserves the distinctions among claims 23, 26, and 29, which recite and claim three fundamentally different methods. *See, e.g.*, *Amgen Inc. v. Hoescht Marion Roussel, Inc.*, 469 F.3d 1039, 1042 (Fed. Cir. 2006) (citing *Modine Mfg. Co. v. ITC*, 75 F.3d 1545, 1556 (Fed. Cir. 1996) ("When claims are amenable to more than one construction, they should when reasonably possible be interpreted so as to preserve their validity.")) (also citing *Smith v. Snow,* 294 U.S. 1, 14 (1935) ("if the claim were fairly susceptible to two constructions, that should be adopted which will secure to the patentee his actual invention")); *see also Phillips v. AWH Corp.*,

415 F.3d 1303, 1327 (Fed. Cir. 2005) (recognizing maxim of construing claims to preserve validity).

2. "A Method For Reducing Deposits in the Final Product During Production of a GLP-1 Agonist Formulation"

a. The Preamble Is an Express Limitation for All of the Reasons Discussed Above and the Following Claim-Specific Reasons

Term	Claims	Novo Nordisk's Construction	Mylan's Construction
"A method for reducing deposits in the final product during production of a GLP-1 agonist formulation"	26, 28	The phrase is an express limitation of claim 23 and it carries its plain and ordinary meaning.	Nonlimiting preamble

For all of the reasons discussed *supra*, "[a] method for reducing deposits in the final product during production of a GLP-1 agonist formulation" should also be construed as an express limitation. *See supra* at Sections IV.A.1.a, IV.A.1.e, IV.A.1.f, IV.A.1.g. The fundamental purpose of the methods of claims 26 and 28 is to reduce deposits in the final product, which is recited in the preambles. *See, e.g.*, D.I. 41, Ex. B, '833 patent at claim 26 ("A method for reducing deposits in the final product during production of a GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein

said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer."). Without the preambles, the claims reduce to replacing a previously used isotonicity agent with propylene glycol—a mere academic exercise. *Boehringer Ingelheim*, 320 F.3d at 1345; *Griffin*, 285 F.3d at 1033; *Vizio, Inc.*, 605 F.3d at 1341.

As with "reducing deposits in production equipment," the specification clearly indicates that "reducing deposits in the final product" is limiting and a necessary component of the claimed inventions. The inventors observed that mannitol resulted in deposits in the final product, which reduced its yield. D.I. 41, Ex. B, '833 patent at col.1, ll.30-45; col.1, ll.39-40. To discover whether a different chemical would not produce deposits in the final product, the inventors conducted a "drop test" with fourteen different chemicals to adjust the tonicity of the formulation and found that propylene glycol, among a few other chemicals, had "suitable properties as replacement[] candidates for mannitol." *Id.* at Example 1. The specification states that the inventors concluded that GLP-1 agonist formulations containing propylene glycol were "optimal for production and for use in injection devices since they exhibit reduced deposits" in the final product. *See, e.g.*, *id.* at Abstract; col.1, ll.15-57; col.2, ll.46-57; col.3, ll.1-30; col.3, ll.39-48; col.14, l.56 – col.15, l.27; Example 1; Figures 1 & 2. Therefore, the specification emphasizes that "[a] method for reducing deposits in the final product during

production of a GLP-1 agonist formulation" is the "essence of the invention" and should be construed as an express limitation as recited in the claims' preambles. *Boehringer*, 320 F.3d at 1345.

The prosecution history also demonstrates that the preamble is an express limitation. In overcoming an obviousness rejection of claims 26 and 28, applicants stressed that the prior art did not mention "a method of reducing deposits." *See* Ex. B at NNVICT-MYL00002617 ("[N]either the Specification, nor any of the examples in [the prior art reference] mention . . . [a] method of reducing deposits or clogging."); Ex. C at NNVICT-MYL00002661. By expressly relying on the preamble to distinguish the claimed invention over the prior art, the prosecution history shows that the preamble to claims 26 and 28 is limiting. *Invitrogen Corp.*, 327 F.3d at 1370.

3. "A Method For Reducing Clogging of Injection Devices By a GLP-1 Agonist Formulation"

a. The Preamble Is an Express Limitation For All of the Reasons Discussed Above and the Following Claim-Specific Reasons

Term	Claims	Novo Nordisk's Construction	Mylan's Construction
"A method for reducing the clogging of injection devices by a GLP-1 agonist formulation"	29, 30, 31	The phrase is an express limitation of claim 23 and it carries its plain and ordinary meaning.	Nonlimiting preamble

For all of the reasons discussed *supra,* "[a] method for reducing the clogging of injection devices by a GLP-1 agonist formulation" should be construed as an express limitation. *See supra* at Sections IV.A.1.a, IV.A.1.e, IV.A.1.f, IV.A.1.g. The fundamental purpose of the methods of claims 29-31 is to reduce clogging of injection devices, which is recited in the preambles. *See, e.g.*, D.I. 41, Ex. B, '833 patent at claim 29 ("A method for reducing the clogging of injection devices by a GLP-1 agonist formulation, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer."). Without the preambles, the claims reduce to replacing a previously used isotonicity agent with propylene glycol—a mere academic exercise. *Boehringer Ingelheim*, 320 F.3d at 1345; *Griffin*, 285 F.3d at 1033; *Vizio, Inc.*, 605 F.3d at 1341.

The specification details that, after the inventors discovered that mannitol clogged injection devices, they performed a number of "clogging tests" with fourteen possible chemicals to adjust the tonicity of the formulation in order to determine whether any of the chemicals produced better results than mannitol. D.I. 41, Ex. B, '833 patent at col.1, ll.30-45; col.1, ll.42-45; Examples 1-4. The results of the clogging test that evaluated all fourteen chemicals are presented in Table 3 of the '833 patent. By conducting these clogging tests, which included a head-to-

head comparison between propylene glycol and mannitol, the inventors discovered that replacing mannitol with propylene glycol in the formulations under investigation resulted in reduced clogging. *Id.*

This testing and finding are reflected in the specification, which states that the GLP-1 agonist formulations containing propylene glycol were "optimal for production and for use in injection devices since they exhibit . . . reduced clogging of injection devices." *See, e.g.*, *id.* at Abstract; col.1, ll.15-57; col.2, ll.58-67; col.3, ll.1-30; col.3, ll.39-48; col.13, ll.30-35; col.13, ll.43-47; col.15, ll.27-56; Examples 1-6; Table 3; Figures 3, 4, & 7. Therefore, the specification emphasizes that "[a] method for reducing the clogging of injection devices by a GLP-1 agonist formulation" is "the essence of the invention" and should be construed as an express limitation as recited in the claims' preambles. *Boehringer*, 320 F.3d at 1345.

The prosecution history also shows this preamble is an express limitation. As with the claims above, in overcoming an obviousness rejection of issued claims 29-31, applicants stressed that the prior art did not disclose or teach "a method of reducing . . . clogging." *See* Ex. B at NNVICT-MYL00002617 ("[N]either the Specification, nor any of the examples in [the prior art reference] mention . . . [a] method of reducing deposits or clogging."); Ex. C at NNVICT-MYL00002661. Again, by expressly relying on the preamble to distinguish the claimed invention

over the prior art, the prosecution history shows that the preamble is limiting. *Invitrogen Corp.*, 327 F.3d at 1370.

B. Defendant's Answering Position

1. SUMMARY OF THE ARGUMENT

There is only one claim construction issue for the Court to consider: Whether a phrase in the preamble of a claim constitutes a claim limitation where the phrase merely recites an intended result, which may or may not occur,[4] of the fully operative method recited in the body of the claim. Each of the disputed preambles merely recites the purpose of the invention—it is "for reducing" particularized manufacturing problems. The method's single step of "replacing the isotonicity agent previously utilized in said formulation with propylene glycol" defines a structurally complete invention absent any reference to that purpose. Preambles are not limiting when a "patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention." *See Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002) (quoting *Rowe v. Dror*, 112 F.3d 473, 478 (Fed. Cir. 1997)); *Arctic Cat Inc. v. GEP Power Prods., Inc.*, 919 F.3d 1320, 1328 (Fed. Cir. 2019). Indeed, this Court has recognized that preambles do not limit the

[4] The claims at issue are not limited to any specific previous isotonicity agent or amounts thereof. Thus, the reductions recited in the claims likely do not occur for the universe of isotonicity agents and concentrations "previously utilized."

method claims of which they are a part, even if the preamble also provides some antecedent basis for the single claimed method step. *Genentech, Inc. v. Amgen Inc.*, No. 17-1407-CFC, 2019 WL 2502932, at *10 (D. Del. June 17, 2019) (holding the preamble phrase "a method for inhibiting VEGF-induced angiogenesis in a subject" to be non-limiting).

2. ARGUMENT

a. Legal Standards

"[P]reambles describing the use of an invention generally do not limit the claims." *Catalina Mktg.*, 289 F.3d at 809. "Whether to treat a preamble term as a claim limitation is determined on the facts of each case in light of the claim as a whole and the invention described in the patent." *Am. Med. Sys., Inc. v. Biolitec, Inc.*, 618 F.3d 1354, 1358 (Fed. Cir. 2010) (internal quotation and citation omitted). The Federal Circuit has explained that "[i]n general, a preamble limits the invention if it recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim." *Catalina Mktg.*, 289 F.3d at 808 (quoting *Pitney Bowes*, 182 F.3d at 1305). "Conversely, a preamble is not limiting 'where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention.'" *Id.* (quoting *Rowe*, 112 F.3d at 478); *Arctic Cat*, 919 F.3d at 1328.

b. The Statements of Purpose and Intended Results in The Preambles of Claims 23, 26, and 29 Do Not Limit the Claims.

The preambles of claims 23, 26, and 29 are not limiting because they merely describe the intended or desired result of the claimed methods without giving life, meaning, and vitality to the claims. This is evidenced by the fact that the preambles at issue simply do not result in a manipulative difference in the claims.

The parties' proposed constructions of the preambles from the claims at issue are set forth below.

Term	Defendant's Position	Plaintiffs' Position
Claim 23: "A method for reducing deposits on production equipment during production of a GLP-1 agonist formulation"	Nonlimiting preamble	The phrase is an express limitation of claim 23 and it carries its plain and ordinary meaning. To the extent a construction is necessary: "A method by which deposits on production equipment are reduced during production of a GLP-1 agonist."
Claim 26: "A method for reducing deposits in the final product during production of a GLP-1 agonist formulation"	Nonlimiting preamble	The phrase is an express limitation of claim 26 and it carries its plain and ordinary meaning. To the extent a construction is necessary: "A method by which deposits in the final product are reduced during production of a GLP-1 agonist formulation."
Claim 29: "A method for reducing the clogging of injection devices by a GLP-1 agonist formulation"	Nonlimiting preamble	The phrase is an express limitation of claim 29 and it carries its plain and ordinary meaning. To the extent a construction is necessary: "A method by which clogging of injection devices caused by a GLP-1 agonist formulation is reduced."

(i) Statements of Purpose or Intended Results Are Not Claim Limitations.

The starting point for any analysis of the construction of preambles of patent claims is the "general rule [that] preamble language is not treated as limiting." *Aspex Eyewear, Inc. v. Marchon Eyewear, Inc.*, 672 F.3d 1335, 1347 (Fed. Cir. 2012); *Catalina Mktg.*, 289 F.3d at 809 ("[P]reambles describing the use of an invention generally do not limit the claims."). That general rule is reinforced when the preamble merely recites a statement of intended use. Claim language that serves only to recite the intended result of a claimed method without altering the steps of the method does not limit the scope of the claim. *See Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1375-76 (Fed. Cir. 2001). This is particularly true "where a patentee defines a structurally complete invention in the claim body and *uses the preamble only to state a purpose or intended use for the invention*." *Catalina Mktg.*, 289 F.3d at 808 (emphasis added) (quoting *Rowe*, 112 F.3d at 478); *Arctic Cat*, 919 F.3d at 1328; *In re Copaxone Consol. Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018) (claim language reciting a potential result, including preambles, not limiting when it does not result in a manipulative difference in the steps of the claims); *Braintree Labs., Inc. v. Novel Labs., Inc.*, 749 F.3d 1349, 1357 (Fed. Cir. 2014) (finding a preamble "not limiting 'where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention'" (quoting *Rowe*,

112 F.3d at 478)); *Takeda Pharm. Co. v. Actavis Labs. FL, Inc*., No. 15-451-RGA, 2016 WL 3193188, at *6-7 (D. Del. June 6, 2016) (finding the preamble phrase "[a] method of treating overweight or obesity having reduced adverse effects" not limiting and merely "extolling benefits or features of the claimed invention" (citations omitted)).

The preambles of the claims at issue here fall squarely into the category of non-limiting statements of intended results. The claim preambles do nothing more than identify the intended results of performing the single step in each claim. The method of claim 23, 26, or 29 is performed *exactly the same way* regardless of whether the intended results are achieved or desired. Claim 23, for example, recites:

> A method for *reducing* **deposits on production equipment during production of a GLP-1 agonist formulation**, said method comprising replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer.

D.I. 41-2 ('833 patent) at 24:7-13 (emphasis added). The only action, or manipulative step, required by the claimed method is "*replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml*." That single step recites the complete method. The bolded phrase, by contrast, does nothing more than identify the purpose and intended results of the method. It tells the person practicing the

method *nothing* about how to perform the method; the preamble has no bearing on what that person does. Thus, the intended results do not limit, qualify, or change the steps of the claimed method and are therefore not limiting. *See In re Copaxone*, 906 F.3d at 1023.

The Court previously considered a similar issue in *Genentech*. There, the claim at issue read:

> A method *for inhibiting VEGF-induced angiogenesis* in a subject, comprising administering to said subject an effective amount of a humanized anti-VEGF antibody which binds human VEGF with a Kd value of no more than about 1x10-8M,
>
> said humanized anti-VEGF antibody comprising a heavy chain variable domain sequence of SEQ ID NO:7 and a light chain variable domain sequence of SEQ ID NO:8.

Genentech, 2019 WL 2502932, at *9. The Court reasoned that the phrase "a method for inhibiting VEGF-induced angiogenesis in a subject" was non-limiting because the claim recites a structurally complete invention in the body and further because the preamble merely recites the purpose of the invention. *Id*. at *10. This was the conclusion even though the term "subject" appeared in both the preamble and the single step in the body of the claim. *Id.*

In another recent case, *In re Copaxone*, the Federal Circuit reviewed a similar question involving claims that included a single manipulative step. As an example, one of the claims at issue in *In re Copaxone* recited:

> *A* ***method of alleviating a symptom of relapsing-remitting multiple sclerosis in a human patient suffering from relapsing-remitting multiple sclerosis or a patient who has experienced a first clinical episode and is determined to be at high risk of developing clinically definite multiple sclerosis*** *comprising administering to the human patient a therapeutically effective regimen of three subcutaneous injections of a 40 mg dose of glatiramer acetate over a period of seven days with at least one day between every subcutaneous injection, the regimen being sufficient to alleviate the symptom of the patient.*

In re Copaxone, 906 F.3d at 1017 (emphasis added). There, the patentee argued that phrases like "alleviating a symptom" were wrongly construed by this Court to be non-limiting. *Id.* at 1023. The Federal Circuit rejected that argument, holding that the many ways that the claims recited a desired therapeutic effect, including in the preambles, did not limit the claims. *Id.* The Federal Circuit held that "[c]laim language without any bearing on the claimed methods should be deemed non-limiting when it does not result in a 'manipulative difference in the steps of the claim.'" *Id.* (quoting *Bristol-Myers Squibb*, 246 F.3d at 1376). The Federal Circuit also noted that none of the statements of intended effect were relied on for patentability during the prosecution history, further reinforcing the conclusion that the statements were non-limiting. *Id.* at 1023-24.

As in *Genentech*, *In re Copaxone*, and other cases cited herein, the preambles of claims 23, 26, and 29 do not result in a manipulative difference in the steps of the claim. The preambles merely describe the intended result of each

claimed method: reduced deposits in production equipment and the final product, and reduced clogging of injection devices.

While a preamble may limit claim scope when it "recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim," *Catalina Mktg.*, 289 F.3d at 808 (citation omitted), that is not the case here. The body of the claims defines a structurally complete invention; the steps of the claimed method vary not at all if the preambles were to be deleted. *TomTom, Inc. v. Adolph*, 790 F.3d 1315, 1324 (Fed. Cir. 2015) ("A preamble is not regarded as limiting ... when the claim body describes a structurally complete invention such that deletion of the preamble phrase does not affect the structure or steps of the claimed invention." (internal quotations and citation omitted)). The methods captured in the body of each claim are performed in exactly the same way regardless of the desired result recited in the claim preambles, and regardless of whether the result is achieved. Irrespective of whether deposits or clogging are actually reduced, each of the claims requires only a step of "replacing the isotonicity agent previously utilized in said formulation with propylene glycol at a concentration of between 1-100 mg/ml." Thus, the preambles fail to satisfy the "life, meaning, or vitality" exception to the rule that preambles are non-limiting.

Plaintiffs' assertion that the preamble is limiting because without them "the claims reduce to … an action that is a meaningless academic exercise with no

purpose in isolation" fails to make the preambles limiting. *Supra* at 17. Plaintiffs generically assert that "reducing deposits on production equipment" is the "*raison d'etre* of the claimed method itself." *Id*. But that is not the test. The purpose, or *raison d'etre* in Plaintiffs' parlance, of the claims at issue in *Genentech* was to inhibit VEGF-induced angiogenesis, but that was still insufficient to render a statement of intended purpose a limitation. This Court thus held that the preamble was "not limiting." *Genentech*, 2019 WL 2502932, at *10.

(ii) Claim Differentiation Does Not Render the Preambles Limiting.

It is of little moment that the bodies of claims 23, 26, and 29 would recite the same language but for the preambles. The doctrine of claim differentiation, i.e., that different claims should have different scope, is merely a guideline; it is not a bright-line rule requiring preambles to be construed as limiting. "The doctrine only creates a presumption that each claim in a patent has a different scope; it is not a 'hard and fast' rule of construction." *Bristol-Myers Squibb*, 246 F.3d at 1376 (declining to "blindly apply the doctrine" even though a non-limiting preamble was the only difference between two claims); *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998) (recognizing "that the doctrine of claim differentiation is not a hard and fast rule of construction" and that it merely "creates a presumption that each claim in a patent has a different scope."). Here, the method is indeed the same regardless of the result desired or achieved.

Neither the specification nor the claims establish that the method differs depending on the desired result in the preamble.

(iii) An Antecedent Basis in the Preamble Does Not Render a Separate Statement of Intended Purpose into a Claim Limitation.

A preamble's statement of intended use is non-limiting even where the body of the claim relies on the preamble for antecedent basis. *CIVIX-DDI, LLC v. Cellco P'ship*, 387 F. Supp. 2d 869, 890 (N.D. Ill. 2005) (citing *Bristol-Myers Squibb*, 246 F.3d 1368). Where preamble language states a purpose or intended use "followed by the body of the claim, in which the claim limitations describing the invention are recited," the preamble may be found non-limiting. *TomTom*, 790 F.3d at 1324.

That the claims here merely refer to a formulation in both the preamble and in the body does not render the whole of the preamble a claim limitation. Merely referring back from the body of the claim to a term in the preamble does not convert the entire "purpose or intended use" portion of the preamble into a claim limitation. *See id.* at 1323 (holding that an entire preamble is not converted into a limitation simply because the body of the claim relies upon a phrase in that preamble); *see also Schumer v. Lab. Computer Sys. Inc.*, 308 F.3d 1304, 1310 (Fed. Cir. 2002) (finding a claim preamble nonlimiting where a portion of the preamble provided antecedent basis for terms in the body of the claim); *Genentech*,

2019 WL 2502932, at *10 (finding preamble nonlimiting, even though a portion of the preamble provided antecedent basis for a term in the body of the claim). The methods recited in the body of each claim here are performed in the identical way regardless of the desired result recited in the claim preambles. The methods do not rely on, or require any context with respect to, a reduction in deposits or clogging.

(iv) The Specification Fails to Support Construing the Preambles as Limiting.

The specification likewise fails to support deeming the preambles as limiting. Plaintiffs assert that Examples 1 and 2 show how "the inventors discovered that propylene glycol reduced deposits in the production equipment during production of a GLP-1 agonist formulation." *Supra* at 18 (citing D.I. 41-2 ('833 patent) at Examples 1 and 2). But these Examples describe neither the use of propylene glycol in a formulation with a GLP-1 agonist, nor replacing one tonicity agent with another.

The description of Example 1 states, for example, that "the screening studies…have been done *using placebo* except where indicated otherwise," based on some undescribed other experiments. D.I. 41-2 ('833 patent) at 16:3-4 (emphasis added). By definition, a placebo formulation lacks the GLP-1 agonist recited in the preambles of claims 23, 26, and 29, and nowhere does Example 1 suggest that the formulations were "otherwise." In fact, only one formulation included both a peptide and an isotonicity agent, and that agent was mannitol; there

is no hint that mannitol was replaced by another isotonicity agent during the experiment. *Id.* at 17:2-4. Further, despite Plaintiffs claiming that improvements in manufacturing were the "essence" or "*raison d'etre*" for the claimed method of using propylene glycol, Example 1 makes clear that propylene glycol was chosen from seven candidate compounds for entirely *different* reasons: propylene glycol had no influence on stability, no influence on antimicrobial preservative testing, and no requirement for further toxicity studies. *Id.* at 18:16-19 (several candidate compounds), 56-67 (reasons for selecting propylene glycol).

Similarly, the title of Example 2 states that it is a "Comparison of Mannitol and Propylene Glycol-Containing *Placebo Formulations* in Simulated Filling Studies and Simulated Use Studies." *Id.* at 19:3-5 (emphasis added). This title makes clear, using the term "placebo," that the formulations of Example 2, by definition, lack the GLP-1 agonist recited in the preambles of claims 23, 26, and 29. Use of the term "comparison" further makes clear that Example 2 does not involving "replacing" one isotonicity agent with another, in a formulation containing a GLP-1 agonist. Thus, neither of the examples relied on by Plaintiffs either shows performance of the claimed method step or achieves the results set forth in the preambles of claims 23, 26, and 29.

Indeed, to the extent the specification deems anything the so-called "essence" of the invention, it was simply to develop formulations containing a

peptide and propylene glycol. Contrary to Plaintiffs' argument, very little of the specification relates to the reduction of deposits and clogging. Any reduction in deposits and clogging was merely a result of properties that the formulations exhibited (and, as noted above, were not the reasons propylene glycol was ultimately selected for the claimed methods). In this sense, the claimed methods have readily apparent utility even without reciting the attributes in the preamble, and the specification reinforces these attributes; namely, propylene glycol's other characteristics that make it a preferred isotonicity agent. *See Sunoco Partners Mktg. & Terminals L.P. v. Powder Springs Logistics, LLC*, No. 17-1390-LPS-CJB, 2019 WL 4051949, at *9 n.10 (D. Del. Aug. 28, 2019) (finding preambles not limiting where "the claims themselves convey processes that have understandable utility"); *see also Wedeco UV Techs., Inc. v. Calgon Carbon Corp.*, No. 01-924 (JAG), 2006 WL 1867201, at *5 (D.N.J. June 30, 2006) (holding that "[t]he preambles do not provide the raison d'etre for the claims" where a method comprising a single step of irradiating water had understandable utility outside the use recited in the preamble), *aff'd*, 223 F. App'x 982 (Fed. Cir. 2007).

Thus, the specification of the '833 patent affirms that the only limitation of any import in the claimed methods is using propylene glycol in place of another isotonicity agent in a peptide formulation, and the preamble recites merely one intended use of this claimed method.

(v) The Prosecution History Fails to Support Construing the Preambles as Limiting.

The prosecution history readily reveals that the patent was allowed based on claim amendments to add a specific buffer. *See supra* 10-12 (Sec. II.B.3). The preambles were already recited in the claims when the claims were rejected. *Id.* Only the addition of the specific buffer to each disputed claim resulted in their allowance. *Id.*

While statements of intended use in a preamble may constitute limitations "if the applicant clearly and unmistakably relied on those uses or benefits to distinguish prior art" (*Catalina Mktg.*, 289 F.3d at 809), that was not the case here. Plaintiffs suggest that the benefit of reduced deposits and clogging was used during prosecution to distinguish these claims against isotonicity agents that were known in the art. But the prosecution history reveals a different story. It was only with the addition of specific excipients to the claims that that Examiner allowed the claims to issue. *See supra* at 10-12 (Sec. II.B.3); *see also In re Copaxone*, 906 F.3d at 1023-24 (noting that the patentee "overstate[d] the intrinsic record" when it suggested that a disputed claim term was the reason the Examiner allowed the claims, but the prosecution history suggested that the term was not "necessary or relevant to the examiner's approval"). Thus, the Court should not construe the preambles to limit the claims.

C. Plaintiffs' Reply Position

1. "A Method For Reducing Deposits on Production Equipment During Production of a GLP-1 Agonist Formulation"[5]

a. Mylan Fails To Rebut That the Preambles Give Life, Meaning, and Vitality to the Claims

Mylan offers no argument for why the "life, meaning, and vitality" inquiry should not apply, aside from conclusory statements that confuse it with a separate inquiry as to whether the preambles recite "essential structure or steps." *Supra* at 30, 37. These are two separate inquires: "a preamble limits the claimed invention if it recites essential structure or steps, **or** if it is necessary to give life, meaning, and vitality to the claims." *In re Cruciferous Sprout Litig.*, 301 F.3d at 1347 (citations omitted) (emphasis added). Conflating the two, Mylan argues that the "life, meaning, or vitality" inquiry is not satisfied because "the steps of the claimed method[s] vary not at all if the preambles were to be deleted." *Supra* at 37. Elsewhere, Mylan asserts that the "life, meaning, and vitality" inquiry is not met because "the preambles at issue simply do not result in a manipulative difference in

[5] Mylan's Answering Claim Construction Brief did not conform to the briefing format required by the Scheduling Order. D.I. 16, ¶ 16. For example, it grouped the three disputed claim terms together into a single argument, making it impossible for Novo Nordisk to reply on a term-by-term basis. Novo Nordisk therefore replies to Mylan's arguments entirely under the heading of this first disputed claim term. Unless otherwise noted, all arguments set forth with respect to this first disputed claim term apply equally to the other disputed claim terms, and will be incorporated by reference in Novo Nordisk's reply position with respect to those terms.

the claims." *Supra* at 31. However, the "life, meaning, and vitality" inquiry is whether the preamble "gives 'life and meaning' *to* the manipulative steps" (*Griffin*, 285 F.3d at 1033 (emphasis added)), not whether it results in a manipulative difference. That is, the inquiry is not whether the preamble adds a manipulative difference or step to the claim, but rather whether it gives "life, meaning, and vitality" to the manipulative steps already present in the claim. Mylan's failure to address this inquiry is no accident. Mylan has no response and as a result, the preambles should be given effect and treated as limitations.

The "life, meaning, and vitality" inquiry perfectly suits the preambles at issue here and confirms they are limiting. The Federal Circuit has held preambles limiting if they give "life and meaning" to the manipulative steps because they are the "essence" of the invention. *Griffin*, 285 F.3d at 1033. A preamble is the "essence" of the claimed invention if, without it, the "performance of the recited steps is nothing but an academic exercise." *Boehringer Ingelheim*, 320 F.3d at 1345; *see also Griffin*, 285 F.3d at 1033. That is the case here. *Supra* at 15-17, 24-25, 27-28.

In interpreting the "life, meaning, and vitality" inquiry, the Federal Circuit has also found preambles limiting if they are not just "merely circumstances in which the method may be useful, but instead are the *raison d'etre* of the claimed method itself." *Boehringer Ingelheim*, 320 F.3d at 1345. Mylan abruptly

dismisses this test as though Plaintiffs had crafted it themselves, not the Federal Circuit. Citing to *Genentech, Inc.*, 2019 WL 2502932, Mylan rejects the *raison d'etre* inquiry as "not the test." *Supra* at 38. However, the *Genentech* Court did not address the "*raison d'etre*" inquiry, and instead applied the "essential steps" inquiry, considering whether the claimed invention was structurally complete without its preamble. But as both parties acknowledge, alternative inquiries exist to determine whether a preamble is limiting. *See supra* at 30-31, 37; *see also Cruciferous Sprout*, 301 F.3d at 1347. The *Genentech* Court's use of the "essential steps" inquiry does not make the "life, meaning, and vitality" or "*raison d'etre*" inquiries any less valid.

Finally, if the preambles at issue here were non-limiting, the scope of the method claims at issue would expand to the bare step of replacing a previously utilized isotonicity agent with propylene glycol. This interpretation cannot be correct because it ignores the essence of the invention, which is the reduction of deposits and clogging. *See Vizio, Inc*, 605 F.3d at 1341 (Fed. Cir. 2010) (finding that the construction "could effectively broaden the claims to cover all devices and methods" involving decoding digital broadcast); *See also On Demand Mach. Corp. v. Ingram Indus.*, 442 F.3d 1331, 1344 (Fed. Cir. 2006) ("The preamble embraces the totality of these limitations, and limits the claim to the subject matter of the preamble.").

b. The Preambles Are Limiting Because They Recite Essential Steps, Without Which the Claims Are Not Structurally Complete

The Court should reject Mylan's argument that the bodies of the claims define structurally complete inventions, while the preambles state only the purpose or intended result. *Supra* at 33-34, 37. The claim bodies—"replacing the isotonicity agent previously utilized in said formulation with propylene glycol"—do not recite structurally complete inventions. Likewise, the preambles do not merely recite purpose or intended result but are necessary to provide a framework for the claimed inventions, i.e., reducing deposits in production equipment, reducing deposits in the final product, and reducing clogging in needles.

The preambles at issue are similar to the preambles in *On Demand Mach. Corp. v. Ingram Indus.*, 442 F.3d 1331 (Fed. Cir. 2006) and in *Deere & Co. v. Bush Hog, LLC*, 703 F.3d 1349 (Fed. Cir. 2012). For example, in *On Demand*, the Federal Circuit found that the preamble phrase, "high speed manufacture of a single copy of book[,]" is limiting because it "serves to focus the reader on the invention that is being claimed" and "necessarily limits the claims, in that it states the framework of the invention." *On Demand*, 442 F.3d at 1343. The Federal Circuit noted that the preamble phrase is "fundamental" to the claimed invention because the specification highlights that a customer may have a printed copy of a book within minutes and therefore, "[t]he preamble embraces the totality of these

inventions, and limits the claim to the subject matter of the preamble." *Id.* at 1343. In *Deere & Co.*, the Federal Circuit found that the term "rotary cutter deck" (which only appeared in the preamble) is limiting because it is "necessary to understand the subject matter encompassed by the claim." *Deere & Co.*, 703 F.3d at 1358. The Federal Circuit further found that this preamble term "does not merely state a name or a use for the claimed [invention,]" but "[r]ather, the term describes a fundamental characteristic of the claimed invention that informs one of skill in the art as to the structure required by the claim." *Id.* (citations omitted).

As in *On Demand* and *Deere & Co.*, the claimed methods here are incomplete without the reductions of deposits and clogging as required by the preambles. The preambles specify where the reductions occur: the production equipment, the final product, and the injection needle. These three elements, found only in the preambles, are required to perform steps of the claims. The specification emphasizes that these elements are important because the entirety of the claimed inventions are directed to reducing deposits and clogging in the production equipment, the final product, and the injection needle. *Poly-America, L.P. v. GSE Lining Tech., Inc.*, 383 F.3d 1303, 1310 (Fed. Cir. 2004) ("Further, when reciting additional structure or steps underscored as important by the specification, the preamble may operate as a claim limitation.") (citation omitted). Therefore, the preambles are limiting because they inform a person of ordinary

skill of the meaning of the replacing step and provide an essential structure to the claims. *Id.* at 1310. (finding that the preamble language "represented an important characteristic of the claimed invention.").

Mylan argues that the preambles at issue here are similar to the ones that were found to be non-limiting in *Genentech* and *In re Copaxone*. *Supra* at 33-35. However, neither case is on point. *Genentech* is distinguishable because the preamble was essentially duplicative of the claim body. In *Genentech*, the body of the claim recited: "administering to [a] subject an effective amount of a humanized anti-VEGF antibody," while the preamble recited: "for inhibiting VEGF-induced angiogenesis in a subject." *Genentech, Inc.*, 2019 WL 2502932, at *10. The court found that the purpose of inhibiting VEG-F induced angiogenesis could be inferred from the administration of an anti-VEGF antibody. Here, however, a person of ordinary skill would not have inferred a reduction in deposits and clogging from the act of replacing a previously utilized isotonicity agent with propylene glycol.

In re Copaxone is not instructive because the terms held to be non-limiting were in the bodies of the claims at issue, and not in their preambles. *In re Copaxone*, 906 F.3d at 1023. Setting that key difference aside, the Court found the term to be non-limiting only because it was "superfluous" of another claim element and "[did] not change the claimed method or require any additional required structure or condition for the claims." *Id.* at 1023. The preambles at issue here are

not superfluous or duplicative of the claim bodies, and instead refer to inventive concepts, which is another reason they are limiting. *Proveris Sci. Corp. v. Innovasystems, Inc.*, 739 F.3d 1367, 1373 (Fed. Cir. 2014) (finding that the preamble "is the only reference in any independent claim to the inventive concept" and that "[t]his fact alone is likely sufficient to support a conclusion that the preamble is limiting").

Finally, citing to *TomTom*, Mylan confuses the "structurally complete" inquiry. *Supra* at 37. The "structurally complete" inquiry considers whether a claimed method would be the same even if the preamble to the claim were deleted. *TomTom*, 790 F.3d at 1324. It is a highly claim-specific inquiry. *Id.* Mylan twists the inquiry to argue that, because the bodies of multiple claims become the same if the preambles are deleted, the preambles are non-limiting. *Supra* at 37 ("The methods captured in the body of each claim are performed in exactly the same way regardless of the desired result recited in the claim preambles, and regardless of whether the result is achieved."). But that is not the test *TomTom* prescribes; it is one that Mylan invented.

Furthermore, in making this argument, Mylan acknowledges that each of claims 23, 26, and 29 would be the same if the preambles were deleted (*supra* at 38-39), thus violating the doctrine of claim differentiation, which provides that no two claims in the same patent should have the same scope. *Comark*

Communications, Inc., 156 F.3d at 1187 (rejecting a construction that would violate claim differentiation). "To the extent that the absence of such difference in meaning and scope would make a claim superfluous, the doctrine of claim differentiation states the presumption that the difference between claims is significant." *Id.* Not only does the "structurally complete" inquiry not produce the result Mylan seeks, Mylan's construction would additionally violate the doctrine of claim differentiation because it would render certain claims superfluous. *Comark Communications*, 156 F.3d at 1187.

c. The Entire Specification Shows That the Preambles Are Limiting

Mylan argues that "very little" of the specification of the '833 patent actually relates to the reduction of deposits and clogging. *See supra* at 42. To the contrary, the entire specification of the '833 patent is directed to the problem of, and solution for, deposits and clogs encountered in working with GLP-1 agonist formulations. *See, e.g.*, '833 patent at col.1, ll.15-57; col.2, ll.35-67; col.3, ll.1-30; col.3, ll.39-48; col.13, ll.30-35; col.13, ll.43-47; col.14, ll.16 – col.15, l.56; Examples 1-4; Table 3; Figures 1-7. This is clear from the '833 patent's title, abstract, background of the invention section, summary of the invention section, and from the patent's Examples and Figures, which demonstrate that reducing deposits and clogging are the essence of the claimed invention. '833 patent at Examples 1-4; Figures 1-7. Mylan cherry-picks certain Examples (i.e., Examples 1

and 2) to allege that the examples do not describe the following: (a) the use of propylene glycol with a GLP-1 agonist (because they instead use placebo formulations) and (b) the step of *replacing* a previously utilized isotonicity agent with propylene glycol. *Supra* at 40-41. According to Mylan, this suggests that the patent's Examples are not truly directed to reducing deposits and clogs.

Mylan is incorrect. First, Example 1 does disclose formulations containing a GLP-1 agonist (i.e., liraglutide). '833 patent at col.17, ll.2-4; col.18, ll.61-63; Figure 1. Specifically, Example 1 states that propylene glycol has "no influence on the physical and chemical stability of [liraglutide]-containing formulations." *Id.* at col.18, ll.61-63. Liraglutide is a GLP-1 agonist. Second, the initial experiments in Examples 1 and 2 did make use of placebo formulations to identify the leading candidates out of a field of thirteen to further test against mannitol. And after the initial battery of tests in Examples 1 and 2 indicated that propylene glycol did reduce deposits and clogging in placebo formulations, the inventors conducted clogging studies with propylene glycol formulations that did contain liraglutide (comparing them to liraglutide formulations containing mannitol) in order to determine whether, in liraglutide formulations, propylene glycol also reduced deposits and clogging (which it surprisingly did). *Id.* at Examples 3-4, Fig. 7. Mylan conveniently ignores Example 3 (and related Figure 7) as well as Example 4, which disclose the results of these clogging studies. *Supra* at 28.

Second, the parties agree that "replacing the isotonicity agent previously utilized in said formulation with propylene glycol" should be construed as "*having a first formulation* that utilized an isotonicity agent other than propylene glycol and *having a second formulation* wherein the isotonicity agent used in the first formulation is substituted or replaced with propylene glycol." *See* D.I. 41, at *1-2 ("The parties . . . jointly propose construction of additional terms from the '833 patent . . . consistent with the constructions recommended by Judge Thynge, and adopted by Judge Bataillon, in" the Teva Litigation), Joint Claim Construction Chart at *4; *Novo Nordisk Inc. v. Teva Pharms. USA, Inc.*, No. 17-227, D.I. 61, at *2 (D. Del. June 26, 2018) (the "*Teva* Litigation") (emphasis added). Yet, in arguing that the '833 patent does not show that "mannitol was replaced by another isotonicity agent during the experiment" because its Examples show only "comparison[s]" of formulations, Mylan ignores the parties' agreed upon construction. *Supra* at 40-41. Mylan also ignores the specification, which shows that the inventors made a "first formulation" with mannitol, which presented problems with deposits and clogging. '833 patent at col.3, ll.30-45. That is, the inventors of the '833 patent set out to find a solution to a problem with the existing mannitol formulation and invented a subsequent propylene glycol formulation, which solved the observed problems. It would be impossible to show a GLP-1 agonist formulation containing mannitol, from which the mannitol was removed

and *replaced* with propylene glycol in the same formulation. To the extent this is Mylan's argument, it should be given no weight.

In any event, the Federal Circuit has found that the title, abstract, and summary of invention in the patent alone may weigh in favor the preambles being limiting. *Poly-America, L.P.*, 383 F.3d at 1310 (finding the preamble limiting because "[t]he specification is replete with references to the invention as a 'blown-film' liner, including the title of the patent itself and the 'Summary of the Invention" and the phrase was "used repeatedly to describe the preferred embodiments" and was "restated in each of the patent's seven claims."); *Deere & Co.*, 703 F.3d at 1358 (finding the preamble limiting because, among other reasons, "[t]he title of the patent, the summary of the invention, and every drawing describe the invention as a deck for a rotary cutter. The specification explains that the invention addresses a concern specific to rotary cutters."). The title, abstract, and summary of invention of the '833 patent also clearly indicate that the preambles at issue are limiting. *See* '833 patent at Title ("Propylene Glycol-Containing Peptide Formulations Which Are Optimal for Production and For Use in Injection Devices"); Abstract ("[t]he present invention further relates to methods for reducing the clogging of injection devices by a peptide formulation and for reducing deposits on production equipment during production of a peptide formulation"); col.3, ll.39-48 ("[t]he pharmaceutical formulations . . . exhibit

reduced deposits in production equipment relative to formulations containing other isotonicity agents as measured by the simulated filling studies described in the Examples" and "exhibit reduced clogging of the injection devices relative to formulations containing other isotonicity agents as measured by the simulated in use studies described in the Examples.").

Mylan also incorrectly argues that the inventors selected propylene glycol for attributes other than its ability to reduce deposits and clogs (i.e., no influence on the physical and chemical stability of liraglutide-containing formulations, no influence on antimicrobial preservative testing, and no further toxicity studies required). *Supra* at 41-42; *see also* '833 patent at col.18, ll.56-67. Propylene glycol was only considered for its other attributes because it first demonstrated an ability to reduce deposits and clogging, which were the problems the inventors were trying to solve. *See, e.g.*, '833 patent at Abstract; col.1, ll.15-57; col.2, ll.35-67; col.3, ll.1-30; col.3, ll.39-48; col.13, ll.30-35; col.13, ll.43-47; col.14, ll.16 – col.15, l.56; Examples 1-4; Table 3; Figures 1-7. The inventors would have never chosen propylene glycol as a replacement candidate for mannitol *but for those reasons*. Propylene glycol continued to advance as a possible, and ultimately the optimal, replacement candidate for mannitol by considering its other attributes identified in Example 1 of the '833 patent. However, its selection was surely not

because of those attributes, as opposed to its ability to reduce deposits and clogs. *See, e.g.*, *id.*

And contrary to Mylan's suggestion, propylene glycol's utility is derived from the intended objective of the preambles (i.e., reducing deposits and clogging). Furthermore, the cases Mylan cites on this point are not instructive because in those cases it was the claim bodies that "clearly articulate what the point of these claimed inventions are." *See Sunoco Partners Marketing & Terminals L.P.*, 2019 WL 4051949, at *9, n.10; *Wedeco UV Techs., Inc.*, 2006 WL 1867201, at *5. In the claims at issue here, it is the preambles, and not the claim bodies, that serve that function. Without the preambles, a person of ordinary skill would not know why to replace a previously utilized isotonicity agent with propylene glycol. In fact, if the first formulation shows no deposits or clogs, a person of ordinary skill would not have a reason to perform the replacing step. Therefore, the disputed preambles are clearly limiting.

d. The Preambles Are Limiting for the Additional Reason That They Are Directed to a New Use of Propylene Glycol: Reducing Deposits and Clogging

The Federal Circuit has found that preambles reciting a new use of a known claim element are limiting. *See, e.g.*, *Cruciferous Sprout*, 301 F.3d at 1348. Although the use of propylene glycol as an excipient may have been known, the preambles are directed to new uses of a propylene glycol in GLP-1 agonist

formulations—reducing deposits and clogging. Therefore, the Court should find them limiting for this additional reason.

The specification states that the inventors were the first to discover that using mannitol in GLP-1 agonist formulations led to problems of deposits and clogging in the production equipment and in injection devices. D.I. 41, Ex. B, '833 patent at col.1, ll.30-45. Since such problems were not known, it follows that reduction of these problems by replacing the previously used isotonicity agent with propylene glycol was a new use for propylene glycol. The prior art does not disclose that mannitol causes, nor that propylene glycol reduces, deposits and clogging.

Catalina Mktg. Int'l v. Coolsavings.com, Inc., 289 F.3d 801 (Fed. Cir. 2002) presents a hypothetical that illustrates why the preambles of claims 23, 26, and 29 are limiting. *Id.* at 809-10. Pursuant to the hypothetical, inventor A receives a patent on a composition claim for a shoe polish. *Id.* at 809. Inventor B would not be able to claim a method of using the composition to shine shoes because the use is not a "new use," but rather the same use. *Id.* Nor could inventor B claim methods of using the polish to repel water on shoes because "repelling water is inherent in the normal use of the polish to shine shoes." *Id.* However, inventor B could claim a method of using the polish to grow hair because it would be a new use. *Id.* at 810. Here, claims 23, 26, and 29 are not directed to known or "normal"

uses of propylene glycol as an excipient. Instead, like using the polish composition to grow hair in *Catalina*, the claims are directed to an entirely different use of propylene glycol—reducing deposits on production equipment and in the final product and reducing clogging in injection needles. And like in *Cruciferous Sprout*, the prior art does not teach this new use. *See Cruciferous Sprout*, 301 F.3d at 1348.

e. Mylan Does Not Deny That the Preambles Provide Antecedent Basis

Mylan alleges that a preamble may be non-limiting even when the body of the claim relies on it for antecedent basis. In doing so, Mylan chooses to ignore the antecedent language of the claims-at-issue, fails to address Novo Nordisk's arguments specific to dependent claims 24, 25, 28, 30, and 31, and relies on inapposite case law. *See supra* at 21-23; *see also supra* at 39-40.

For example, Mylan cites to *CIVIX-DDI, LLC. v. Cellco Partnership*, 387 F. Supp. 2d 869, 890 (N.D. Ill. 2005) to argue that preambles may be non-limiting despite providing antecedent basis. *Supra* at 39. But *CIVIX-DDI* does not even decide this issue, and instead orders additional briefing. Mylan further relies on *Schumer*, which is easily distinguishable. The preambles in *Schumer* describe a feature that necessarily exists in the coordinate system described in the claim bodies, whereas the preambles at issue here do not describe features existing in the bodies of the claims-at-issue. *See Schumer*, 308 F.3d at 1310. Instead, the

preambles call for a person of ordinary skill to first assess deposits and clogging in a first formulation before performing the replacing step. Absent the presence of deposits or clogs, there would be no reason to perform the replacing step. Thus, the content of the preambles here is not necessarily present in the replacing step in the bodies of the claims. Therefore, the preambles are necessary to provide antecedent basis. *Supra* at 21-23.

In the remaining cases Mylan cites, antecedent basis was not the sole factor considered in determining whether the preamble was limiting. *See Genentech, Inc.*, 2019 WL 2502932, at *10; *TomTom*, 790 F.3d at 1324. The preambles at issue here provide clear antecedent basis, (*supra* at 21-23), but even without this additional reason, the intrinsic evidence, including claim language, the specification, and the prosecution history, resoundingly show that the preambles are limiting.

f. The Prosecution History Does Not Support Mylan, But Rather Shows That the Preambles Are Limiting

There is no requirement that the Examiner distinguish the preamble from the prior art during prosecution for it to be limiting. Regardless of what the Examiner cited in the Notice of Allowance, the *applicants* expressly relied on the preamble to distinguish the claimed invention over the prior art. *See* Ex. B at NNVICT-MYL00002617 ("[N]either the Specification, nor any of the examples in [the prior

art reference] mention . . . [a] method of reducing deposits or clogging."); Ex. C at NNVICT-MYL00002661; *see also Invitrogen Corp.*, 327 F.3d at 1370.

Nonetheless, independent of the prosecution history, the claims and the entirety of the specification demonstrate that the disputed preambles should be construed as limiting. *See, e.g.*, *Boehringer Ingelheim*, 320 F.3d at 1345 (finding that the preamble is limiting without addressing the prosecution history); *Griffin*, 285 F.3d at 1033 (same); *Proveris*, 739 F.3d at 1372-73 (same); *Poly-America, L.P.*, 383 F.3d at 1310; *Bicon*, 441 F.3d at 952-53; *On Demand*, 442 F.3d at 1324.

2. "A Method For Reducing Deposits in the Final Product During Production of a GLP-1 Agonist Formulation"

Novo Nordisk incorporates by reference its reply position set forth above with respect to the claim term "[a] Method For Reducing Deposits on Production Equipment During Production of a GLP-1 Agonist Formulation." *Supra* Section IV.C.1.

3. "A Method For Reducing Clogging of Injection Devices By a GLP-1 Agonist Formulation"

Novo Nordisk incorporates by reference its reply position set forth above with respect to the claim term "[a] Method For Reducing Deposits on Production Equipment During Production of a GLP-1 Agonist Formulation." *Supra* Section IV.C.1.

In particular, Examples 3 and 4 (and Figure 7) of the patent's specification present the results of "clogging tests," which showed that replacing mannitol with propylene glycol in the GLP-1 formulations under consideration reduced clogging of injection devices, expressly refuting Mylan's assertion that the Examples relied on by Novo Nordisk do not show performance of the claimed methods. *Supra* Section IV.C.1.c; *see supra* at 28-29; *see also supra* at 40-41.

D. Defendant's Sur-Reply Position

1. The PTAB Held that the Preambles Are Not Limiting

The PTAB recently instituted Mylan's petition for *inter partes* review of the '833 patent. Ex. 5. In its institution decision, the PTAB agreed that the preambles are nonlimiting:

> [W]e agree with [Mylan] that the preambles of claims 23, 26, and 29 are not limiting. The recitation of "reducing deposits on production equipment," "reducing deposits in the final product," and "reducing the clogging of injection devices" merely state the purpose or intended use of the claimed subject matter without reciting essential structure or steps, and have not been shown to be "necessary to give life, meaning, and vitality" to the claims.

Id. at 8. The PTAB "applie[d] the same claim construction standard that would be used to construe the claim in a civil action…." *Id.* at 7. The PTAB's holding thus reinforces Mylan's construction.

2. The Preambles Merely Recite Intended Results of a Complete Method

The claimed method recites a single step—replacing a first isotonicity agent with propylene glycol. In contrast, the preambles recite only what *could* happen when a formulation's existing isotonicity agent is replaced with propylene glycol. The disputed claims recite a complete invention without resort to the preambles for any life, meaning, or vitality.

Plaintiffs analogize the preambles here to those in *Deere & Co. v. Bush Hog, LLC*, 703 F.3d 1349 (Fed. Cir. 2012), and *On Demand Machine Corp. v. Ingram Industries, Inc.*, 442 F.3d 1331 (Fed. Cir. 2006), but neither analogy is persuasive. The *Deere* preamble recited a physical component of a claimed device, without which the remaining structure lacked meaning. 703 F.3d at 1358. The preambles used the term "rotary cutter deck," which described a "fundamental characteristic of the claimed invention" to inform one of skill in the art as to the claim's required structure. *Id.* The claim body made little sense if the term "rotary cutter deck" was not a limitation. The *On Demand* preambles recited the "high speed manufacture of a single copy of a book." 442 F.3d at 1343. The claimed method centered around the fast manufacture of a single copy of a book and involved numerous steps, distinguished in the specification from a large-scale commercial process. *Id.* at 1343-44. Neither case bears on the issues here.

Here, unlike *On Demand* and *Deere*, the preambles are not fundamental characteristics of the claimed invention. As Mylan explained, the methods recited in the bodies of claims 23, 26, and 29 of the '833 patent are complete; performed the same way *regardless* of whether the preambles' intended results are achieved or desired. *Supra* at 34-38 (Sec. IV.B.2.b.(i)). Moreover, Plaintiffs fail to connect the preambles to the bodies of the claims at issue.

The parties' agreement as to the construction of the "replacing" term provides no support for treating the preambles as limitations. Using that construction in claim 23, the method recites:

> A method for reducing deposits on production equipment during production of a GLP-1 agonist formulation, said method comprising [*having a first formulation that utilized an isotonicity agent other than propylene glycol and*
> *having a second formulation wherein the isotonicity agent in the first formulation is substituted or replaced with propylene glycol*]
> at a concentration of between 1-100 mg/ml, and wherein said GLP-1 agonist formulation comprises a disodium phosphate dihydrate buffer.

D.I. 41-2 ('833 patent) at 24:7-13 (construction inserted; line breaks for clarity). The agreed construction says nothing about reduced deposits, and the preamble does not fill in any details of the claimed substituting a first isotonicity agent with propylene glycol. Instead, the preambles merely recite the intended results of the substitution.

Furthermore, Plaintiffs' assertion that the preambles at issue here are not akin to those at issue in *Genentech* and *In re Copaxone* is incorrect. Regarding *Genentech*, Plaintiffs assert that "[t]he court found that the purpose of inhibiting VEG-F induced angiogenesis could be inferred from the administration of an anti-VEGF antibody." *Supra* at 49. But the Court's holding in *Genentech* was that the preamble was not limiting because "claim 2 recites a structurally complete invention" and the preamble "merely recites the purpose of the invention." *Genentech, Inc. v. Amgen Inc.*, No. 17-1407-CFC, 2019 WL 2502932, at *10 (D. Del. June 17, 2019). Even if Plaintiffs were correct, the rule of *Genentech* would not help them because both conditions are present here.

With respect to *In re Copaxone*, Plaintiffs assert that "the terms held to be non-limiting were in the bodies of the claims at issue, and not in their preambles." *Supra* at 49. Plaintiffs are incorrect: The Federal Circuit rejected the patentee's argument that claim terms, including in the preambles, were wrongly construed by this court to be nonlimiting. *In re Copaxone Consol. Cases*, 906 F.3d 1013, 1023 (Fed. Cir. 2018) (ruling on the preambles of claims 5, 12, and 16 of U.S. Patent No. 9,155,776). Plaintiffs misinterpret the Federal Circuit's opinion by stating that "the Court found the term to be non-limiting *only* because it was 'superfluous' of another claim element and '[did] not change the claimed method or require any additional required structure or condition for the claims.'" *Supra* at 49 (emphasis

added) (quoting *In re Copaxone*, 906 F.3d at 1023). The rule of *Copaxone* fits the facts here: language is not limiting when it "does not change the … method already disclosed in the claims, or otherwise result in a manipulative difference in the steps of the claims." 906 F.3d at 1023.

Finally, Plaintiffs misstate Mylan's argument with respect to the "structurally complete" inquiry described by the Federal Circuit in *TomTom*. Plaintiffs assert that "Mylan confuses the 'structurally complete' inquiry … The 'structurally complete' inquiry considers whether a claimed method would be the same even if the preamble to the claim were deleted." *Supra* at 50. That is exactly what Mylan stated in its Answering Brief: "The body of the claims defines a structurally complete invention; the steps of the claimed method vary not at all if the preambles were to be deleted." *Supra* at 37. Thus, to assert that "Mylan invented" the test described in Mylan's Answering Brief, as quoted directly from *TomTom*, is incorrect. The simple fact is that each of claims 23, 26, and 29 recites a complete method of a single step, which is not changed by the intended results recited in each claim's preamble.

Accordingly, Plaintiffs fail to rebut Mylan's position that the preambles are nothing more than the intended result of each claimed method and should be found nonlimiting.

3. The Preambles Do Not Give Life, Meaning, and Vitality to the Claims

Plaintiffs assert that "Mylan offers no argument for why the 'life, meaning, and vitality' inquiry" does not apply here and that Mylan "confuse[s] it with a separate inquiry as to whether the preambles recite 'essential structure or steps.'" *Supra* at 44. Plaintiffs' argument misses the mark for at least two reasons. *First*, the Federal Circuit made clear that a preamble is not limiting if the body of a claim defines a structurally complete invention and the preamble merely recites an intended use. *See Arctic Cat Inc. v. GEP Power Prods., Inc.*, 919 F.3d 1320, 1328 (Fed. Cir. 2019) ("We have long ruled that 'a preamble is not limiting "where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention."'" (quoting *Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc.*, 289 F.3d 801, 808 (Fed. Cir. 2002))); *see also Georgetown Rail Equip. Co. v. Holland L.P.*, 867 F.3d 1229, 1236–37 (Fed. Cir. 2017); *Deere*, 703 F.3d at 1358. Here, the preambles of the claims merely recite an intended use for the complete single-step method recited in the body of each claim. *Supra* at 31-38 (Sec. IV.B.2.b.(i)).

Second, Plaintiffs' attempt to construct a two-part inquiry out of the *Catalina* language overstates that decision. *Supra* at 44 (Sec. IV.C.1.a) ("These are two separate inquires: 'a preamble limits the claimed invention if it recites essential structure or steps, **or** if it is necessary to give life, meaning, and vitality to

the claims.'" (first quoting *In re Cruciferous Sprout Litig.*, 301 F.3d 1343, 1347 (Fed. Cir. 2002); and then quoting *Catalina*, 289 F.3d at 808)). *Catalina* did not go so far: *Catalina* held that the preambles there were nonlimiting *without* asking whether the preambles breathed "life, meaning, and vitality" into the claims, after finding simply that the "claim body defines a structurally complete invention." *See also* Ex. 6 (Manual of Patent Examining Procedure § 2111.02) (stating that "[t]he determination of whether a preamble limits a claim is made on a case-by-case basis in light of the facts in each case; there is no litmus test defining when a preamble limits the scope of a claim" (citing *Catalina*, 289 F.3d at 808)).

4. The Intrinsic Evidence Supports the Conclusion that the Preambles are Not Limiting

a. The Claims

Plaintiffs assert that because the claims "would be the same if the preambles were deleted," the doctrine of claim differentiation applies. But claim differentiation "is not a 'hard and fast' rule of construction." *See*, *e.g.*, *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1376 (Fed. Cir. 2001) (quoting *Comark Commc'ns, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998)). Both the Federal Circuit and courts in this district decline to apply the doctrine in situations, like this, where the facts warrant. *Bristol-Myers*, 246 F.3d at 1376; *In re Copaxone 40 mg*, No. 14-1171-GMS, 2016 WL 873062, at *1 n.2 (D.

Del. Mar. 7, 2016) ("the doctrine of claim differentiation alone cannot save claims that do not contain any true limitations").

Similarly, Plaintiffs fail to rebut Mylan's position, which has been adopted by this Court, that a preamble does not become a claim limitation merely because it provides minimal antecedent basis. *Genentech*, 2019 WL 2502932, at *10. Plaintiffs attempt to distinguish controlling case law by arguing that the preambles here "call for a person of ordinary skill to first assess deposits and clogging in a first formulation before performing the replacing step."[6] *Supra* at 59. But the preambles in no way require that "assessment." Plaintiffs also waived that argument by failing to propose such a construction.

Accordingly, the structure of claims 23, 26, and 29 of the '833 patent supports the conclusion that the preambles at issue are not claim limitations.

b. The Specification

Plaintiffs assert that "the entire specification of the '833 patent is directed to the problem of, and solution for, deposits and clogs encountered in working with GLP-1 agonist formulations." *Supra* at 51. Plaintiffs further assert that "Mylan cherry-picks certain Examples (i.e., Examples 1 and 2)" to suggest that the

[6] Claims must be construed identically for both infringement and validity. *TVIIM, LLC v. McAfee, Inc.*, 851 F.3d 1356, 1362 (Fed. Cir. 2017). To the extent Plaintiffs' construction is adopted, Plaintiffs should be held to their representations as to what the preambles require to be infringed.

Examples described in the specification are not directed to reducing deposits and clogs. *Supra* at 51-52. Plaintiffs are wrong on both counts. *First*, the specification is directed toward more than just the reduction of deposits and clogging, *supra* at 40-42 (Sec. IV.B.2.b.(iv)), as the patent's Abstract shows (D.I. 41-2 at abstract).

Second, Mylan did not "cherry-pick" Examples 1 and 2 to discuss from the specification: those are the only Examples Plaintiffs relied on in their opening brief, *see supra* at 17-19 (Sec. IV.A.1.c), and Mylan showed how those examples do not support Plaintiffs' position because "only one formulation included both a peptide and an isotonicity agent, and that agent was mannitol; there is no hint that mannitol was replaced by another isotonicity agent during the experiment." *Supra* at 40-41. Moreover, only Examples 1-2 are cited by Plaintiffs as supporting intrinsic evidence for claims 23 and 26 in the *Joint Claim Construction Chart* (D.I. 41). Plaintiffs' reliance on new intrinsic evidence to suggest the specification was cherry-picked is not supportable. From 24 columns of text, including six Examples and seven Figures, Plaintiffs' opening-brief "essence" argument relied on roughly two Examples, two Figures, and a few column excerpts. *Supra* at 17-19 (Sec. IV.A.1.c).

Plaintiffs next assert "that the title, abstract, and summary of invention in the patent alone may weigh in favor [of] the preambles being limiting." *Supra* at 54 (citing *Poly-Am., L.P. v. GSE Lining Tech., Inc.*, 383 F.3d 1303, 1310 (Fed. Cir.

2004)). First, Plaintiffs' brief shows that *Poly-America* was not so limited, because it analyzed a specification "replete with references to the invention," and a phrase "used repeatedly to describe the preferred embodiments" and "restated in each of the patent's seven claims." *Id.* (quoting *Poly-Am.*, 383 F.3d at 1310). Second, the '833 patent identifies multiple aspects of the alleged inventions beyond the few mentioned in claims 23, 26, and 29: the Abstract states that the invention relates to formulations comprising a peptide and propylene glycol, methods of preparing formulations, and uses of formulations in the treatment of diseases and conditions; the written description contains ten full columns of detail about alternative embodiments of claimed formulations and species of GLP-1 agonists; and 22 of the patent's 31 claims recite pharmaceutical formulations and methods of making them. D.I. 41-2 ('833 patent) at abstract, 3:33-13:29, 22:47-24:6. Thus, the '833 patent as a whole supports the conclusion that the preambles do not reflect an "essence" of the invention.

c. The Prosecution History

Plaintiffs also failed to rebut Mylan's argument that the prosecution history plainly shows that the Examiner allowed the '833 patent to issue because of claim amendments that added a specific buffer, not because of the content of the preamble. Plaintiffs set aside the Examiner's Notice of Allowance as irrelevant, asserting that the Examiner need not have relied on the preambles for them to limit

the claims. *Supra* at 59-60 (Sec. IV.C.1.f). But that misdirects the inquiry. The issue is that the Examiner did not rely on the preambles to allow the claims, thereby lending support to the notion that the preambles are not limitations. *See In re Copaxone*, 906 F.3d at 1024 (rejecting argument that certain language limited the claims because it was neither necessary nor relevant to allowance in the face of other amendments); *Symantec Corp. v. Computer Assocs. Int'l, Inc.*, 522 F.3d 1279, 1289 (Fed. Cir. 2008) ("prosecution history fail[ed] to demonstrate 'clear reliance on the preamble during prosecution to distinguish the claimed invention from the prior art'" where the preamble language "did not have its own independent significance" among multiple amendments (citation omitted)). Because the Examiner allowed the claims to issue only after applicants added specific excipients to the claims, *supra* at 43, the prosecution history strongly supports the conclusion that the preambles are not claim limitations.

5. The Preambles do not Describe a New Use of Propylene Glycol

Plaintiffs introduce a new argument in their Reply Brief that "the preambles are directed to new uses of a propylene glycol in GLP-1 agonist formulations—reducing deposits and clogging." *Supra* at 56-57. To the extent the Court does not find this argument waived, it is also incorrect. The prior art disclosed that solutions using mannitol as an isotonicity agent exhibited precipitation, salting out, and/or flocculation. *See*, *e.g.*, Epperson, *Mannitol Crystallization in Plastic*

Containers, 35 AM. J. HOSPITAL PHARMACY 1337 (1978) (Ex. 7); Jacobs, *Factors Influencing Drug Stability in Intravenous Infusions*, 27 J. HOSP. PHARM. 341 (1969) (Ex. 8). The prior art also taught that using propylene glycol would alleviate these problems. *See, e.g.*, Powell, *Parenteral Peptide Formulations: Chemical and Physical Properties of Native Luteinizing Hormone-Releasing Hormone (LHRH) and Hydrophobic Analogues in Aqueous Solution*, 8 PHARM. RESEARCH 1258 (1991) (Ex. 9). Thus, as in *Bristol-Myers*, the claimed statements of intended results recited in the preambles are not limitations because they recite results known in the prior art. 246 F.3d at 1375-76.

V. CONCLUSION

A. Plaintiffs' Position

For the forgoing reasons, the Court should adopt Novo Nordisk's proposed claim constructions.

B. Defendant's Position

Defendants respectfully request that the Court adopt Mylan's construction and hold that the preambles of claims 23, 26, and 29 are non-limiting.

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